REMARKS

Amendment to the Specification and Claims

The specification amendment corrects a clerical error in the attribution of a SEQ ID NO, and does not add new matter. Amendments to the claims, further described below, add no new matter.

The Office Action

Prior to entry of the foregoing amendments, claims 27-46 and 52 were pending in the application and rejected on various grounds.

Claims 37 and 43 - 46 are canceled by amendment herein without prejudice.

Claims 27 - 36, 38 - 41, and 52 are amended herein for the reasons advanced below, and additionally to correct obvious typographical errors in claim 35 ("gutamine (Q)" to "glutamine (Q)") and claim 36 ("cystine (C)" to "cysteine (C)"), bringing the textual description of the respective amino acid into conformity with the single letter amino acid code. No new matter has been added.

Claims 27 - 36, 38 - 42, and 52 are presented for further examination.

All rejections and objections are respectfully traversed.

Claim Rejections - 35 U.S.C. § 112

(a) Scope of Enablement

The Examiner rejects claims 41 - 42, drawn to a method of inhibiting the binding of a DM2 protein to a p53 protein, under 35 U.S. § 112, first paragraph, for inadequate scope of enablement. Acknowledging that applicants' specification is "enabling for methods of inhibiting DM2 protein binding to p53 in vitro," the Examiner asserts that the specification nonetheless "does not reasonably provide enablement for methods of inhibiting the binding of DM2 and p53 in vivo."

The Examiner posits that "results achieved in vitro, using purified proteins in defined solutions, are not representative or correlative of achieving . . . binding inhibition in a target cell

in vivo," and from that unsupported proposition summarily concludes that it would require undue experimentation "to determine the appropriate means of delivery, dosage and concentration to inhibit DM2 and p53 binding in appropriate target cells in any organism comprising administration of the polypeptides claimed."

The Examiner has the initial burden of challenging a presumptively enabling disclosure. "[I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain ***why*** it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own ***with acceptable evidence or reasoning*** which is inconsistent with the contested statement." *In re Marzocchi*, 439 F.2d 220, 224 (C.C.P.A. 1971) (emphasis added); *quoted with approval in In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995) .

The Examiner's conclusory statements are neither such evidence nor such reasoning.

Indeed, the Examiner's assertion that "results achieved in vitro, using purified proteins in defined solutions, are not representative or correlative of achieving . . . binding inhibition in a target cell in vivo," is precisely the type of unsupported allegation that has been explicitly disapproved and held inadequate to support a *prima facie* case of nonenablement: the examiner "***must give reasons*** for a conclusion of lack of correlation for an in vitro . . . model. " M.P.E.P. § 2164.02 (8th ed., rev. 2) (citing to *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985)) (emphasis added).

This, the Examiner has not done, and on this basis alone the rejection is in error and should be withdrawn.

Furthermore, it is the disclosure of the specification, *coupled* with information known in the art as of the priority date, that must enable the claims; a patent need not teach, and preferably omits, what is well known in the art. M.P.E.P. § 2164.01 (8th ed., rev. 2).

As noted in applicants' prior response, WO 96/02642 (IDS Reference # AH) and corresponding U.S. Pat. No. 6,153,391 ("the '391 patent") are part of the state of that art, the '391 patent evincing the PTO's prior, *binding*, determination that p53-derived peptides are fully able to inhibit p53-MDM2 interaction *in vivo*.[1]

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[1] Claim 1 of the '391 patent, reproduced in relevant part in applicants' prior response, reads on both in vivo and in vitro methods for the same reasons that the Examiner has advanced

In order to establish a *prima facie* case that the instant specification, coupled with the information in that prior art, provides inadequate scope of enablement, the Examiner must provide acceptable evidence and reasoning why one skilled in the art would reasonably doubt that the peptides of the instant invention, *in specific contrast* to those set forth in the '391 patent, would not reasonably be expected to inhibit interaction of p53 and MDM2 in vivo.

This, the Examiner has manifestly failed to do. The rejection is in error and should be withdrawn.

(b) Lack of Enablement

The Examiner rejects claims 43 - 46, drawn to a purification method, for lack of enablement under 35 U.S.C. § 112, ¶ 1.

Without acceding to the accuracy or propriety of the rejection, and solely to expedite prosecution, applicants herein cancel claims 43 - 46, obviating the rejection. Applicants thus respectfully request that the rejection be withdrawn.

(c) Indefiniteness

Claims 43 - 46 stand rejected under 35 U.S.C. § 112, second paragraph on grounds of indefiniteness. For the reasons advanced above, applicants have canceled claims 43 - 46, thus obviating the rejection. Applicants respectfully request that the rejection be withdrawn.

(d) Written Description

Applicants acknowledge with appreciation the Examiner's withdrawal of the prior written description rejection focused on the amino acid motifs of the peptides of applicants' claims. But in a new rejection under 35 U.S.C. § 112, first paragraph, the Examiner rejects claims

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with respect to the claims in the instant application. The claims of the '391 patent are presumptively valid, 35 U.S.C. § 282, and are thus presumed by statute to satisfy all requirements of 35 U.S.C. § 112, first paragraph. The Examiner is bound by this prior correct determination of the Office. M.P.E.P. § 1701.

27 - 46 and 52 as lacking written description adequate to support the genus of "compounds" and, with respect to claim 30, additionally rejects the claim for inadequate written description support for the genus of "cyclic lactams."

Applicants respectfully traverse the rejections.

In the first of the two rejections, the Examiner suggests that "the specification and claims do not indicate what distinguishing attributes are concisely shared by the members of the genus comprising compounds that bind to DM2 protein, and which further comprise the amino acid sequences claimed." The statement is self-contradictory: the distinguishing attributes ***are*** the recited amino acid sequences and the functional requirement that the compounds bind to DM2 protein.

And such distinguishing attributes suffice to describe the claimed genus, providing "partial structure", "functional characteristics . . . coupled with a . . . disclosed correlation between function and structure, [and] . . . some combination of such characteristics." *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement*, 66 Fed. Reg. 1099, 1106 (2001), adopted as persuasive authority by *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316 (Fed. Cir. 2002) ("Enzo *II*").[2] That the genus is "very broad" is itself of no moment.

Nonetheless, in order to expedite prosecution, and explicitly reserving the right to prosecute claims of the examined scope in one or more continuation applications, applicants herein amend the claims to recite a genus of "peptide[s]", rather than "compounds", and respectfully submit that the written description in applicants' specification is commensurate in scope with the claims as herein amended.

In a second rejection, the Examiner posits that the recitation in claim 31 that the amino acid motif of the claimed compound comprises a cyclic lactam "reads on non-amino acid structures such as uric acid."

Although applicants believe that the intended scope of the claim as examined is clear, and that the written description in the specification is adequate to support that claim, applicants

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[2] This is especially so in light of the scope of the claims issued in the '391 patent, drawn to use of "compounds" comprising a p53 peptide fragment.

amend the claim herein to clarify that the claimed compound is a peptide that *is* a cyclic lactam. Written description support for the claim as herein amended can be found, for example, in the substitute specification at p. 6, lines 6 - 25, particularly lines 15 - 25.

Applicants respectfully submit that the rejection has been obviated by amendment and should be withdrawn.

Claim Rejections - 35 U.S.C. § 102

Claims 27, 28, 38, 41, 42 and 52 have been rejected as anticipated by portions of the sequence of the Chinese hamster p53 protein, Lee *et al.*, Gene 184:177-183 (1997) (hereinafter, "Lee").

The rejection is based on a misreading of the reference: the cited sequences from Lee all have the wild-type Leu (L) residue at R_3, rather than His (H), Phe (F) or Tyr (Y) as required by applicants' claims.

Lacking an element of applicants' claims, the reference does not anticipate, and applicants respectfully request that the rejection be withdrawn.

CONCLUSION

All claims pending in this application are believed to be *prima facie* in condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39749-0002APC). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Dated: AUG 13, 2004

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